Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1.-46. **(Cancelled)**

47. (New) A non-human transgenic animal having (i) a transgene integrated into the genome of the animal and (ii) a *tet* operator-linked gene of interest in the genome of the animal, wherein:

(a) the transgene comprises a transcriptional regulatory element functional in cells of the animal operatively linked to a polynucleotide sequence encoding a fusion protein which inhibits transcription in eukaryotic cells; and

(b) the fusion protein comprising a first polypeptide, which is a Tet repressor or mutated Tet repressor that binds to a *tet* operator sequence, operatively linked to a heterologous second polypeptide which inhibits transcription in eukaryotic cells,

wherein: (i) the transgene is expressed in cells of the animal at a level sufficient to produce amounts of the fusion protein that are sufficient to inhibit transcription of the *tet* operator-linked gene, and (ii) the level of transcription of the *tet* operator-linked gene is upon regulation less than the level of transcription prior to regulation by the fusion protein.

48. (New) The animal of claim 47, wherein the first polypeptide of the fusion protein is a Tet repressor that binds to *tet* operator sequences in the absence but not the presence of tetracycline or a tetracycline analogue.

49. (New) The animal of claim 48, wherein the first polypeptide comprises an amino acid sequence shown in SEQ ID NO 17.

50. (New) The animal of claim 47, wherein the first polypeptide of the fusion protein is a mutated Tet repressor that binds to *tet* operator sequences in the presence but not the absence of tetracycline or a tetracycline analogue.

51. (New) The animal of claims 50, wherein the mutated Tet repressor has at least one amino acid substitution compared to a wild-type Tet repressor.

52. (New) The animal of claim 51, wherein the mutated Tet repressor has an amino acid substitution at least one amino acid position corresponding to an amino acid position selected from the group consisting of position 71, position 95, position 101 and position 102 of a wild-type Tn10-derived Tet repressor amino acid sequence.

53. (New) The animal of claim 52, wherein the mutated Tet repressor comprises an amino acid sequence shown in SEQ ID NO: 19.

54. (New) The animal of claim 47, wherein the second polypeptide comprises a transcription silencer domain of a protein selected from the group consisting of v-erbA, the Drosophila Krueppel protein, the retinoic acid receptor alpha, the thyroid hormone receptor alpha, the yeast Ssn6/Tupl protein complex, the Drosophila protein even-skipped, SIRI, NeP1, the Drosophila dorsal protein, TSF3, SF1, the Drosophila hunchback protein, the Drosophila knirps protein, WT1, Oct-2.1, the Drosophila engrailed protein, E4BP4, and ZFS.

55. (New) The animal of claim 47, which is selected from the group consisting of a cow, a goat, a sheep, a mouse, a monkey, a dog, a cat, a rabbit, a rat, and a pig.

56. (New) The animal of claim 47, wherein the transgene is integrated at a predetermined location within a chromosome within cells of the animal.

57. (New) The animal of claim 47, wherein expression of the transgene is regulated by at least one *tet* operator sequence.

58. (New) The animal of claim 47, wherein expression of the transgene is regulated by at least one tissue-specific regulatory element.

59. (New) The animal of claim 47, wherein the *tet* operator-linked gene is a second transgene comprising a gene of interest operably linked to at least one *tet* operator sequence.

60. (New) The animal of claim 59, wherein the at least one *tet* operator sequence is operatively linked upstream of the second transgene.

61. (New) The animal of claim 59, wherein the at least one *tet* operator sequence is operatively linked downstream of the second transgene.

62. (New) The animal of claim 47, wherein the *tet* operator-linked gene is an endogenous gene that has been operatively linked to at least one *tet* operator sequence.

63. (New) A method for modulating transcription of the *tet* operator-linked gene in the transgenic animal of claims 47, comprising administering tetracycline or a tetracycline analogue to the animal.

64. (New) A non-human transgenic animal having (i) a transgene integrated into the genome of the animal and (ii) a *tet* operator-linked gene in the genome of the animal, wherein:

(a) the transgene comprises a transcriptional regulatory element functional in cells of the animal operatively linked to a polynucleotide sequence encoding a fusion protein which inhibits transcription of said *tet* operator linked gene;

(b) said fusion protein comprises a first polypeptide which is a Tet repressor operably linked to a heterologous second polypeptide which inhibits transcription of said *tet* operator-linked gene in eukaryotic cells;

(c) said *tet* operator-linked gene is expressed at detectable levels in cells of the animal in the presence of tetracycline or an analogue thereof;

(d) said transgene is expressed in cells of the animal at a level sufficient to produce amounts of said fusion protein that are sufficient to inhibit transcription of the *tet* operator-linked gene; and

(e) in the absence of tetracycline or a tetracycline analogue in the animal, said fusion protein binds to the *tet* operator-linked gene and inhibits transcription of the tet operator linked gene, wherein the level of expression of the *tet* operator-linked gene can be upregulated by administering tetracycline or a tetracycline analogue to the animal.

65. (New) The animal of claim 64, wherein the first polypeptide comprises an amino acid sequence shown in SEQ ID NO 17.

66. (New) The animal of claim 64, wherein the second polypeptide comprises a transcription silencer domain of a protein selected from the group consisting of v-erbA, the Drosophila Krueppel protein, the retinoic acid receptor alpha, the thyroid hormone receptor alpha, the yeast Ssn6/Tupl protein complex, the Drosophila protein even-skipped, SIRI, NeP1, the Drosophila dorsal protein, TSF3, SF1, the Drosophila hunchback protein, the Drosophila knirps protein, WT1, Oct-2.1, the Drosophila engrailed protein, E4BP4, and ZFS.

67. (New) The animal of claim 64, which is selected from the group consisting of a cow, a goat, a sheep, a mouse, a monkey, a dog, a cat, a rabbit, a rat, and a pig.

68. (New) A method for modulating transcription of the *tet* operator-linked gene in the transgenic animal of claim 64, comprising administering tetracycline or a tetracycline analogue to the animal.

69. (New) A non-human transgenic animal having a transgene integrated into the genome of the animal and also having a *tet* operator-linked gene in the genome of the animal, wherein:

(a) the transgene comprises a transcriptional regulatory element functional in cells of the animal operatively linked to a polynucleotide sequence encoding a fusion protein which inhibits transcription of said *tet* operator linked gene;

(b) said fusion protein comprises a first polypeptide that is a mutated Tet repressor that binds to *tet* operator sequences in the presence, but not the absence, of tetracycline or a tetracycline analogue, operably linked to a heterologous second polypeptide which inhibits transcription of said tet operator-linked gene in eukaryotic cells;

(c) said *tet* operator-linked gene is expressed at detectable levels in cells of the animal in the absence of tetracycline or an analogue thereof;

(d) said transgene is expressed in cells of the animal at a level sufficient to produce amounts of said fusion protein that are sufficient to inhibit transcription of the *tet* operator-linked gene; and

(e) in the presence of tetracycline or a tetracycline analogue in the animal, said fusion protein binds to the *tet* operator-linked gene and inhibits transcription of the tet operator linked gene, wherein the level of expression of the *tet* operator-linked gene can be upregulated by depleting tetracycline or a tetracycline analogue from the animal.

70. (New) The animal of claim 69, wherein the mutated Tet repressor has at least one amino acid substitution compared to a wild-type Tet repressor.

71. (New) The animal of claim 69, wherein the second polypeptide comprises a transcription silencer domain of a protein selected from the group consisting of v-erbA, the Drosophila Krueppel protein, the retinoic acid receptor alpha, the thyroid hormone receptor alpha, the yeast Ssn6/Tupl protein complex, the Drosophila protein even-skipped, SIRI, NeP1, the Drosophila dorsal protein, TSF3, SF1, the Drosophila hunchback protein, the Drosophila knirps protein, WT1, Oct-2.1, the Drosophila engrailed protein, E4BP4, and ZFS.

72. (New) The animal of claim 69, which is selected from the group consisting of a cow, a goat, a sheep, a mouse, a monkey, a dog, a cat, a rabbit, a rat, and a pig.

73. (New) A method for modulating transcription of the *tet* operator-linked gene in the transgenic animal of claim 69, comprising administering tetracycline or a tetracycline analogue to the animal.

74. (New) A transgenic non-human animal having a transgene integrated into the genome of the animal, wherein:

(a) the transgene comprises a transcriptional regulatory element functional in cells of the animal operatively linked to a polynucleotide sequence encoding a fusion protein which inhibits transcription of a in operator linked gene; and

(b) the fusion protein comprises a first polypeptide that is a Tet repressor or a mutated Tet repressor that binds to a *tet* operator sequence, operatively linked to a second polypeptide which inhibits transcription in eukaryotic cells, and

(c) said fusion protein is expressed in cells of the animal.

75. (New) The animal of claim 74, wherein the first polypeptide of the fusion protein binds to *tet* operator sequences in the absence but not the presence of tetracycline or a tetracycline analogue.

76. (New) The animal of claim 75, wherein the first polypeptide is a Tet repressor.

77. (New) The animal of claim 75, wherein the first polypeptide comprises an amino acid sequence shown in SEQ ID NO: 17.

78. (New) The animal of claim 74, wherein the first polypeptide of the fusion protein binds to *tet* operator sequences in the presence but not the absence of tetracycline or a tetracycline analogue.

79. (New) The animal of claim 78, wherein the first polypeptide is a mutated Tet repressor.

80. (New) The animal of claim 79, wherein the mutated Tet repressor has at least one amino acid substitution compared to a wild-type Tet repressor.

81. (New) The animal of claim 79, wherein the mutated Tet repressor has an amino acid substitution at least one amino acid position corresponding to an amino acid position selected from the group consisting of position 71, position 95, position 101, and position 102 of a wild-type TnlO-derived Tet repressor amino acid sequence.

82. (New) The animal of claim 79, wherein the mutated Tet repressor comprises an amino acid sequence shown in SEQ ID NO: 19.

83. (New) The animal of claim 74, wherein the second polypeptide comprises a transcription silencer domain of a protein selected from the group consisting of v-erbA, the Drosophila Krueppel protein, the retinoic acid receptor alpha, the thyroid hormone receptor alpha, the yeast Ssn6/Tupl protein complex, the Drosophila protein evenskipped, SIRI, NeP1, the Drosophila dorsal protein, TSF3, SF1, the Drosophila hunchback protein, the Drosophila knirps protein, WT1, Oct-2.1, the Drosophila engrailed protein, E4BP4, and ZF5.

84. (New) The animal of claim 74, wherein the *tet* operator-linked gene is a second transgene comprising a gene of interest operably linked to at least one tet operator sequence.

85. (New) The animal of claim 74, which is selected from the group consisting of a cow, a goat, a sheep, a mouse, a monkey, a dog, a cat, a rabbit, a rat, and a pig.